REMARKS

Claims 1 and 20 have been amended. New Claims 26-28 have been added. Accordingly, claims 1-21 and 25-28 are pending. Support for the amendment and new claims is found throughout the specification and claims as originally filed. For example, the amendment to Claim 1 is supported by the specification at page 14, lines 9-12. The amendment to Claim 20 is supported by the specification at page 13, lines 11-23. New Claim 26 is supported by the specification at page 9, lines 8-12. New Claims 27-28 are supported by the specification at page 10, lines 12-13 and 20. Accordingly, no new matter has been added.

In response to the Office Action mailed on March 5, 2010, Applicants submit the following remarks.

Withdrawal of Rejections

Applicants gratefully acknowledge the withdrawal of rejections under 35 U.S.C. § 101, 35 U.S.C. § 112, second paragraph, 35 U.S.C. § 102(b) and 35 U.S.C. §103(a).

Rejection of Claims 1, 2, 4-8, 10, 11, 14, 17, 19 and 21 under 35 U.S.C. § 103(a)

The Examiner has rejected Claims 1, 2, 4-8, 10, 11, 14, 17, 19 and 21 under 35 U.S.C. § 103(a) as allegedly being unpatentable over Forster et al. (AU52162/96, hereinafter "Forster") in view of Hennessy (U.S. 5,840,324, hereinafter "Hennessy") as evidenced by Lau et al. (WO 2004/069242, hereinafter "Lau"). Specifically, the Examiner asserts Forster teaches combinations of anthelmintics. The Examiner acknowledges that Forster does not teach an intraruminal bolus device, stepwise method or efficacy duration. However, the Examiner alleges that such features are taught by Hennessy. The Examiner thus concludes that it would have been obvious to one of ordinary skill in the art to utilize the composition of Forster in combination with the continuous release allegedly taught by Hennessy.

Applicants note that the present technology relates to a controlled release device that delivers the equivalent of a high dose every day for a period of 3 to 14 days, long enough to provide extremely high efficacy against parasites, but not long enough to build up resistance in worm populations. Specification at page 13, lines 19-23. Thus, a key advantage of the claimed methods is that the combined force of multiple anthelmintics at high dosage achieves high

efficacy against resistant genotypes in order to delay development of resistant populations. This effect is achieved by delivering the multiple anthelmintics in the form of a bolus which is targeted towards and remains within the rumen of the animal. Specification at page 14, lines 9-12. Accordingly, Applicants submit that the instant claims are not obvious for the following reasons.

1. The prior art references, either alone or when combined, fail to teach or suggest all of the elements of independent Claim 1.

The law dictates that in order to establish a *prima facie* case of obviousness, among other things, the prior art must teach or suggest all the claim limitations. (M.P.E.P. § 2143).

Forster and Hennessy, either alone or when combined, fail to teach or suggest all of the elements of independent Claim 1, or any of the claims dependent thereon. Specifically, neither Forster nor Hennessy teach or suggest "an intra-ruminal bolus configured to release from the rumen an effective amount of active agents each day for a period of between 3 and 14 days," as recited in amended Claim 1.

Intra-ruminal bolus. The Examiner concedes that Forster does not teach an intra-ruminal bolus device, and asserts that Hennessy teaches an intra-ruminal bolus. However, Hennessy relates to "finely dispersed particles" containing a single active agent. *See* Hennessy at Example 1. Thus, contrary to the assertions in the Office Action, the finely dispersed particles of Hennessy can not be considered a bolus. Because Hennessy teaches the use of finely dispersed particles, Hennessy fails to disclose an intra-ruminal bolus, as recited in Claim 1.

Furthermore, the finely dispersed particles of Hennessy are not targeted to the rumen, but instead are designed to pass into the abomasum and small intestine. The purpose of the particles of Hennessy is to delay release of the active agent until the particles reach the abomasum and small intestine. It is not surprising, therefore, that Hennessy states that "it is crucial that absorption from the rumen be controlled and restricted." Hennessy at column 2, lines 61-63. In contrast, amended Claim 1 recites, in relevant part, delivering "an intra-ruminal bolus configured to release from the rumen an effective amount of active agents each day for a period of between 3 and 14 days." Because Hennessy does not disclose the use of an intra-ruminal bolus, Hennessy fails to teach, suggest or in any way make obvious each of the elements of amended Claim 1.

Release from the rumen. The Examiner concedes that Forster does not teach efficacy duration, and asserts that Hennessy discloses this feature. Although Applicants maintain that neither Forster nor Hennessy disclose the claimed subject matter, solely in an effort to expedite prosecution, Applicants have amended Claim 1 to recite that the release of active agent occurs "from the rumen." Accordingly, Applicants submit that neither Forster nor Hennessy disclose a device that releases from the rumen an effective amount of active agents each day for a period of between 3 and 14 days. Hennessy teaches that the mean residence time of materials in the rumen is about 10 hours. *See* Hennessy at Example 2. Hennessy also teaches that "it is crucial that absorption from the rumen be controlled and restricted." Hennessy at column 2, lines 61-63. In contrast, amended Claim 1 recites, in relevant part, delivering "an intra-ruminal bolus configured to release from the rumen an effective amount of active agents each day for a period of between 3 and 14 days." Because the particles of Hennessy are designed to pass out of the rumen within a mean time of 10 hours, Hennessy fails to disclose the extended release from the rumen recited in amended Claim 1. Accordingly, Hennessy fails to teach, suggest or in any way make obvious each of the elements of amended Claim 1.

Accordingly, even when combined, none of the cited references, alone or combined, teaches all of the elements of the claimed invention, including delivering "an intra-ruminal bolus configured to release from the rumen an effective amount of active agents each day for a period of between 3 and 14 days," as recited in Claim 1 as amended. Because the cited references fail to teach each and every element of Claim 1, a *prima facie* case of obviousness has not been established.

2. The cited art teaches away from the claimed method.

In addition to the above, Applicants submit that the cited reference teaches away from the claimed method. Specifically, Hennessy teaches that "it is crucial that absorption from the rumen be controlled and restricted." Hennessy at column 2, lines 61-63. Additionally, Hennessy teaches that reducing absorption from the rumen is important because the dosages of agents absorbed from the rumen "are of little additional value." Hennessy at column 3, lines 1-14. Furthermore, Hennessy teaches active agent should be released with anywhere from 5 to 30 times greater availability in the small intestine compared to the rumen. Hennessy at column 5, lines

34-44. Thus, one of skill in the art would not have been motivated by the teaching of Hennessy to utilize a bolus which remains within the rumen of the animal, as recited in amended Claim 1. Instead, one of skill in the art would have been motivated to restrict release from the rumen and use particles which release active agent in the small intestine. Accordingly, for at least this reason, a *prima facie* case of obviousness has not been established.

3. The claimed method meets a long-felt unmet need.

In addition to the above, Applicants submit that the claimed method addresses a long-felt unmet need. In particular, Applicants note that the efficacy of any anthelmintic product against resistant worms is a key factor in delaying the development of severe, production-limiting resistance. The problem of anthelmintic-resistant parasites in sheep and goats has continued to worsen in many countries. See Specification at page 1, line 15 – page 2, line14. However, although there has been a growing need for treatments that delay the development of resistant parasites, this great need had gone unmet by available treatments until the development of the presently-claimed method. Specifically, as noted in the instant specification:

> It was shown as early as 1978 ... that extending the period over which worms are exposed to benzimidazole drenches increases their efficacy. ...
>
> Thus, despite having known for 25 years that extending the duration of worm exposure to some actives can substantially increase efficacy there has never been a product produced which fully capitalizes on this knowledge. Further, the only product on the market for sheep and cattle ... lasts for 100 days, resulting in long withholding periods for the ivermectin variant.
>
> Furthermore, the prolonged delivery of small doses of anthelmintic may actually select for resistance in the worm population.

See Specification at page 3, lines 6-8 and page 4, line 23 – page 5, line 4. As such, the specification makes clear at least two key points. First, since at least 1978, there has been an acknowledgment by those of ordinary skill in the art of the need for increased efficacy against resistant parasites, without further selecting for resistant populations. Second, because the only product on the market as of Applicants' effective filing date actually increased selection for resistance in worm populations, there had been a failure of others to satisfy this unmet need.

Finally, Applicants note that there has been a significant level of research and development into new anthelimintics, formulations and techniques by expert parasitologists throughout the world for many years. However, the instant application represents the first time that anyone had successfully combined the use of: i) two or more active agents at ii) high enough doses to effectively reduce the level of parasites while iii) minimizing the undue selection of resistant populations that occurs during long-term exposure to small doses of active agent. Accordingly, because the method of the instant claims addresses a long-felt unmet need in the art, Applicants respectfully submit that the instant claims are not obvious under 35 U.S.C. § 103(a).

In light of the foregoing, Applicants submit that Claims 1, 2, 4-8, 10, 11, 14, 17, 19 and 21 are not obvious under 35 U.S.C. § 103(a). Applicants respectfully request withdrawal of this rejection and allowance of the pending claims.

Rejection of Claims 3, 9, 20 and 25 under 35 U.S.C. § 103(a)

The Examiner rejects Claims 3, 9, 20 and 25 under 35 U.S.C. § 103(a) as allegedly being unpatentable over Forster in view of Hennessy as evidenced by Lau, and further in view of Whitehead (U.S. 6,030,637, hereinafter "Whitehead"). Specifically, the Examiner rejects Claims 3, 9, 20 and 25, alleging that although Forster or Hennessy do not teach the recited features, such features are taught by Whitehead. Regarding Claims 3 and 25, the Examiner alleges that Whitehead teaches continuous release of active agents. Regarding Claim 9, the Examiner alleges that Whitehead teaches use of abamectin in a dose of 0.2 mg/kg in combination with other anthelmintics for treating sheep. Regarding Claim 20, the Examiner alleges that Whitehead teaches a maximum integral dose. The Examiner then concludes that it would have been obvious to one of ordinary skill in the art to utilize the anthelmintic compositions of Forster and Hennessy in combination with the features allegedly taught by Whitehead. Applicants disagree.

Regarding the rejection of Claims 3, 9, 20 and 25 in general, Applicants respectfully submit that Whitehead does not render the claims obvious. Specifically, as discussed above, one of skill in the art would not have been motivated by the teaching of Hennessy to utilize a bolus which remains within the rumen of the animal, because Hennessy teaches that absorption from

the rumen should be restricted, and that the dosages of agents absorbed from the rumen "are of little additional value." Thus, one of skill in the art would have been motivated by Hennessy to restrict release from the rumen and use particles which release active agent in the small intestine. The teaching of Whitehead does not change the fact that Hennessy teaches away from the claimed method, and thus, there would have been no motivation to combine the teachings of Whitehead in the methods of Forster or Hennessy. Accordingly, for at least this reason, a *prima facie* case of obviousness has not been established.

Additionally, regarding the rejection of Claim 9, Applicants respectfully submit that Whitehead does not teach dose ranges of abamectin. Contrary to the assertions at page 7 of the Office Action, Whitehead does not teach specific dosages of abamectin, and does not teach abamectin in combination with other anthelmintic active agents for treating sheep. Because Whitehead fails to teach the specific dose ranges of abamectin, Whitehead fails to teach or suggest all of the claim limitations. Accordingly, for at least this reason, a *prima facie* case of obviousness has not been established.

Rejection of Claim 12 under 35 U.S.C. § 103(a)

The Examiner rejects Claim 12 under 35 U.S.C. § 103(a) as allegedly being unpatentable over Forster in view of Hennessy as evidenced by Lau, and further in view of IVS Annual Index of Veterinary Products (hereinafter "IVS"). Specifically, the Examiner asserts that although Hennessy does not teach the dosage of albendazole recited in claim 12, such dose range is taught by IVS. The Examiner then concludes that the dosage quantity disclosed by IVS would have rendered the claimed dose range obvious. Applicants disagree.

Applicant maintains that Claim 12 is not obvious over Froster in view of Hennessy and further in view of IVS because none of these references, either alone or combined, teach or suggest all the limitations of any of these claims. As discussed above in the response to the rejection under 35 U.S.C. § 102(b), Hennessy fails to teach the element of "an intra-ruminal bolus configured to release from the rumen an effective amount of active agents each day for a period of between 3 and 14 days." Applicant respectfully submits that IVS fails to remedy this defect. At best, IVS teaches an effective dosage for a single anthelmintic agent. However, IVS fails to teach "an intra-ruminal bolus configured to release from the rumen an effective amount of

active agents each day for a period of between 3 and 14 days," as recited in claim 1 as amended. Because IVS fails to teach this missing feature, IVS fails to teach or suggest all of the claim limitations. Accordingly, for at least this reason, a *prima facie* case of obviousness has not been established.

Applicants therefore submit that Claim 12 is not obvious under 35 U.S.C. § 103(a). Applicants respectfully request withdrawal of this rejection and allowance of the pending claims.

Rejection of Claim 13 under 35 U.S.C. § 103(a)

The Examiner rejects Claim 13 under 35 U.S.C. § 103(a) as allegedly being unpatentable over Forster in view of Hennessy as evidenced by Lau, and further in view of Sanyal (Vet. Res. Comm. 20, 1996, 461-468, hereinafter "Sanyal"). Specifically, the Examiner asserts that although Hennessy does not teach the use of tricalbendazole, such use is taught by Sanyal as a low-level intraruminal anti-fluke agent. The Examiner then concludes that it would have been obvious to one of ordinary skill in the art to use triclabendazole disclosed by Sanyal in the bolus of Hennessy. Applicants disagree.

Applicant maintains that Claim 13 is not obvious over Forster in view of Hennessy as evidenced by Lau and further in view of Sanyal because neither of these references, either alone or combined, teach or suggest all the limitations of any of these claims. As discussed above in the response to the rejection under 35 U.S.C. § 102(b), Hennessy fails to teach the element of "an intra-ruminal bolus configured to release from the rumen an effective amount of active agents each day for a period of between 3 and 14 days." Applicant respectfully submits that Sanyal fails to remedy this defect. At best, Sanyal teaches use of triclabendazole as an anthelmintic agent. However, Sanyal fails to teach "an intra-ruminal bolus configured to release from the rumen an effective amount of active agents each day for a period of between 3 and 14 days," as recited in claim 1 as amended. Because Sanyal fails to teach this missing feature, Sanyal fails to teach or suggest all of the claim limitations. Accordingly, for at least this reason, a *prima facie* case of obviousness has not been established.

Applicants therefore submit that Claim 13 is not obvious under 35 U.S.C. § 103(a). Applicants respectfully request withdrawal of this rejection and allowance of the pending claims.

Rejection of Claims 15, 16 and 18 under 35 U.S.C. § 103(a)

The Examiner rejects Claims 15, 16 and 18 under 35 U.S.C. § 103(a) as allegedly being unpatentable over Forster in view of Hennessy as evidenced by Lau, and further in view of Sanyal. Specifically, regarding claims 15 and 16, the Examiner asserts that although Forster and Hennessy do not teach the timed release of antiparasite active agents for the claimed time periods, such time periods are taught by Sanyal. Regarding claim 18, the Examiner asserts that although Hennessy does not explicitly teach treatment of ecto-parasites, such activity is disclosed by Sanyal. The Examiner then concludes that one of ordinary skill in the art would have expected reasonable success from limiting the temporal time period of release to the range disclosed by Sanyal. Applicants disagree.

As an initial matter, Applicants note that although the Examiner applies the combined teachings of Forster, Hennessy and Sanyal, the rejection is confusing because the Examiner discusses passages from Lewis as allegedly disclosing the subject matter of the rejected claims. However, the Examiner concludes that one of skill in the art would have been motivated to apply the teachings of Sanyal to the combined disclosure of Forster and Hennessy. *See* Office Action at page 10, last two paragraphs.

Applicant maintains that Claims 15, 16 and 18 are not obvious over Forster in view of Hennessy as evidenced by Lau, and further in view of Sanyal because none of these references, either alone or combined, teach or suggest all the limitations of any of these claims. As discussed above, neither Forster nor Hennessy teach or suggest "an intra-ruminal bolus configured to release from the rumen an effective amount of active agents each day for a period of between 3 and 14 days." The disclosure of Sanyal fails to remedy this deficiency. At best, Sanyal teaches use of triclabendazole as an anthelmintic agent. However, Sanyal fails to teach "an intra-ruminal bolus configured to release from the rumen an effective amount of active agents each day for a period of between 3 and 14 days," as recited in amended Claim 1. Because Sanyal fails to teach this missing feature, Sanyal fails to teach or suggest all of the claim

limitations. Accordingly, for at least this reason, a *prima facie* case of obviousness has not been established.

Applicants therefore submit that Claims 15, 16 and 18 are not obvious under 35 U.S.C. § 103(a). Applicants respectfully request withdrawal of this rejection and allowance of the pending claims.

Double Patenting

The Examiner provisionally rejects claims 1, 3, 15 and 16 on the ground of nonstatutory double patenting over claims 1-4 and 20 of copending Application No. 11/908,708. Applicants will consider submitting a terminal disclaimer to overcome the rejection of Claims 1, 3, 15 and 16 once claims 1, 3, 15 and 16 of the instant application are found to be otherwise allowable.

No Disclaimers or Disavowals

Although the present communication may include alterations to the application or claims, or characterizations of claim scope or referenced art, Applicant is not conceding in this application that previously pending claims are not patentable over the cited references. Rather, any alterations or characterizations are being made to facilitate expeditious prosecution of this application. Applicant reserves the right to pursue at a later date any previously pending or other broader or narrower claims that capture any subject matter supported by the present disclosure, including subject matter found to be specifically disclaimed herein or by any prior prosecution. Accordingly, reviewers of this or any parent, child or related prosecution history shall not reasonably infer that Applicant has made any disclaimers or disavowals of any subject matter supported by the present application.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

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